

## APPENDIX B

### Interfering Smith and Engelhardt Claims Corresponding to Count 1

<u>Proposed Count 1</u>	<u>Smith Claim 1</u>	<u>Engelhardt Claim 1768</u>	<u>Why the Claims Interfere</u>
<p>A method of separating and detecting tagged polynucleotides which comprises:</p> <p style="text-align: center;"><i>or</i></p> <p>A process for resolving or separating non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:</p>	<p>A method of separating and detecting tagged polynucleotides which comprises:</p>	<p>A process for resolving or separating non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:</p>	<p>Smith Claim 1 anticipates or renders obvious Engelhardt Claim 1768 and vice versa because both claims recite a method for “separating” and “detecting” “tagged” (Smith Claim 1) or “non-radioactively labeled” (Engelhardt Claim 1768) nucleic acids. Although the preamble recitation in Engelhardt Claim 1768 does not mention “detecting,” the body of the claim recites that the separated fragments are detected. Thus, there is no patentable distinction between these two claim limitations.</p>
<p>providing a plurality of polynucleotides, each tagged with a chromophore or fluorophore;</p> <p style="text-align: center;"><i>or</i></p> <p>providing or generating detectable non-radioactively labeled nucleic acid fragments comprising one or more nucleotides that may be attached to, or coupled to, or incorporated into DNA or RNA, and wherein one or more fluorescent indicators are covalently attached, directly or through a linkage group, to the furanosyl</p>	<p>providing a plurality of polynucleotides, each tagged with a chromophore or fluorophore;</p>	<p>providing or generating detectable non-radioactively labeled nucleic acid fragments comprising one or more nucleotides that may be attached to, or coupled to, or incorporated into DNA or RNA, and wherein one or more fluorescent indicators are covalently attached, directly or through a linkage group, to the furanosyl</p>	<p>Smith Claim 1 anticipates or renders obvious Engelhardt Claim 1768 and vice versa because polynucleotides tagged with a chromophore or fluorophore (Smith Claim 1) include nucleic acid fragments labeled with one or more fluorescent indicators (Engelhardt Claim 1768). Thus, there is no patentable distinction between these two claim limitations.</p>

<u>Proposed Count 1</u>	<u>Smith Claim 1</u>	<u>Engelhardt Claim 1768</u>	<u>Why the Claims Interfere</u>
coupled to, or incorporated into DNA or RNA, and wherein one or more fluorescent indicators are covalently attached, directly or through a linkage group, to the furanosyl moiety, the phosphate moiety, the base moiety of said nucleotides, or any combination thereof;		moiety, the phosphate moiety, the base moiety and said nucleotides, or any combination thereof;	
resolving to separate one of the plurality of tagged polynucleotides from the other tagged polynucleotides differing in length by a single nucleotide using an electrophoretic procedure capable of resolving tagged polynucleotides differing by a single nucleotide; and  or subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and	resolving to separate one of the plurality of tagged polynucleotides from the other tagged polynucleotides differing in length by a single nucleotide using an electrophoretic procedure capable of resolving tagged polynucleotides differing by a single nucleotide; and	subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and	Smith Claim 1 anticipates or renders obvious Engelhardt Claim 1768 and vice versa because “resolving to separate” the tagged polynucleotides “using an electrophoretic procedure capable of resolving tagged polynucleotides differing by a single nucleotide” (Smith Claim 1) is merely an alternative way of stating, “subjecting said detectable non-radioactively labeled fragments to a sequencing gel to separate or resolve said fragments” (Engelhardt Claim 1768). One of skill in the art would recognize that subjecting a labeled polynucleotide fragment to a sequencing gel means employing an electrophoretic procedure to resolve and separate the fragments. Thus, there is no patentable distinction between these two claim limitations.

<u>Proposed Count 1</u>	<u>Smith Claim 1</u>	<u>Engelhardt Claim 1768</u>	<u>Why the Claims Interfere</u>
<p>detecting the resolved tagged polynucleotides by means of the chromophore or fluorophore.</p> <p><i>or</i></p> <p>detecting non-radioactively said separated or resolved fragments by means of said fluorescent indicators attached to said nucleotides.</p>	<p>detecting the resolved tagged polynucleotides by means of the chromophore or fluorophore.</p>	<p>detecting non-radioactively said separated or resolved fragments by means of said fluorescent indicators attached to said nucleotides.</p>	<p>Smith Claim 1 anticipates or renders obvious Engelhardt Claim 1768 and vice versa because “detecting the resolved tagged polynucleotides by means of the chromophore or fluorophore” (Smith Claim 1) and “detecting non-radioactively said separated or resolved fragments by means of said fluorescent indicators attached to said nucleotides” (Engelhardt Claim 1768) are merely alternative ways of stating the same thing. Thus, there is no patentable distinction between these two claim limitations.</p>

<u>Proposed Count 1</u>	<u>Smith Claim 14</u>	<u>Engelhardt Claim 1795</u>	<u>Why the Claims Interfere</u>
<p>A method of separating and detecting tagged polynucleotides which comprises:</p> <p><i>or</i></p> <p>A process for resolving or separating non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:</p>	<p>A method of determining the sequence of a polynucleotide by analyzing polynucleotide fragments generated by a polynucleotide sequencing technique, each of said polynucleotide fragments being tagged with a chromophore or fluorophore, comprising:</p>	<p>A process for determining the sequence of a nucleic acid of interest comprising: providing or generating detectable non-radioactively labeled nucleic acid fragments comprising: (a) a sequence complementary to said nucleic acid of interest or a portion thereof, and (b) fluorescent labels covalently attached, directly or through a linkage group, to said fragments;</p>	<p>Smith Claim 14 anticipates or renders obvious Engelhardt Claim 1795 and vice versa because both claims recite a method for "determining the sequence" of a "polynucleotide" (Smith Claim 14) or "nucleic acid of interest" (Engelhardt Claim 1795). Furthermore, Smith Claim 14 recites that the polynucleotide fragments are "tagged with a chromophore or fluorophore," and Engelhardt Claim 1795 recites that the nucleic acid fragments comprise "fluorescent labels." Since "polynucleotide" and "nucleic acid" are synonymous and since "fluorophore or chromophore" anticipates "fluorescent label," and vice versa, no patentable distinction between these two claim limitations exists.</p>
<p>providing a plurality of polynucleotides, each tagged with a chromophore or fluorophore;</p> <p><i>or</i></p> <p>providing or generating detectable non-radioactively labeled nucleic acid fragments comprising one or more nucleotides</p>	<p>introducing the tagged polynucleotide fragments into an electrophoretic medium; separating the tagged polynucleotide fragments in said electrophoretic medium using an electrophoretic procedure capable of resolving said polynucleotide fragments</p>	<p>subjecting said labeled fragments to a sequencing gel to separate or resolve said labeled fragments;</p>	<p>Smith Claim 14 anticipates or renders obvious Engelhardt Claim 1795 and vice versa because "introducing" and "separating the tagged polynucleotide fragments... using an electrophoretic procedure capable of resolving said polynucleotide fragments differing in length by a single nucleotide" (Smith Claim 14) is merely an alternative way of stating "subjecting said labeled fragments to a sequencing gel to separate or resolve said labeled fragments" (Engelhardt Claim 1795).</p>

<u>Proposed Count 1</u>	<u>Smith Claim 14</u>	<u>Engelhardt Claim 1795</u>	<u>Why the Claims Interfere</u>
that may be attached to, or coupled to, or incorporated into DNA or RNA, and wherein one or more fluorescent indicators are covalently attached, directly or through a linkage group, to the furanosyl moiety, the phosphate moiety, the base moiety of said nucleotides, or any combination thereof;	differing in length by a single nucleotide;		One of skill in the art would recognize that subjecting a labeled polynucleotide fragment to a sequencing gel means employing an electrophoretic procedure to resolve and separate the fragments. Thus, there is no patentable distinction between these two claim limitations.
resolving to separate one of the plurality of tagged polynucleotides from the other tagged polynucleotides differing in length by a single nucleotide using an electrophoretic procedure capable of resolving tagged polynucleotides differing by a single nucleotide; and  or subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and	detecting the separated tagged polynucleotide fragments by means of the chromophore or fluorophore; and determining the polynucleotide sequence from the polynucleotide fragments detected.	detecting non-radioactively said separated or resolved fragments by means of said attached fluorescent labels; and determining the sequence of said nucleic acid of interest from said detected fragments.	Smith Claim 14 anticipates or renders obvious Engelhardt Claim 1795 and vice versa because “detecting the separated tagged polynucleotide fragments by means of the chromophore or fluorophore” (Smith Claim 14) and “detecting non-radioactively said separated or resolved fragments by means of said fluorescent labels” (Engelhardt Claim 1795) are merely alternative ways of stating the same thing. Furthermore, as explained in the text above, both Smith Claim 14 and Engelhardt Claim 1795 correspond to Count 1 because the count renders obvious both claims. Since the only practical purpose at the time of the Smith invention for detecting polynucleotides differing in length by a single nucleotide was to determine the

<u>Proposed Count 1</u>	<u>Smith Claim 14</u>	<u>Engelhardt Claim 1795</u>	<u>Why the Claims Interfere</u>
			polynucleotides' sequence, it would have been obvious to one skilled in the art to determine the sequence of the polynucleotides once they had been detected.